

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

1-29. (Canceled)

30. (Previously Amended) A method for modifying the glycosylation profile of a polypeptide produced by a mammalian host cell, comprising introducing into said host cell an isolated nucleic acid comprising a sequence encoding a fusion polypeptide, wherein said fusion polypeptide has $\beta(1,4)$ -N-acetylglucosaminyltransferase III activity and comprises the Golgi localization domain of a Golgi resident polypeptide other than $\beta(1,4)$ -N-acetylglucosaminyltransferase III, and wherein said modified polypeptide has increased Fc-receptor binding or effector function as a result of said modification.

31. (Previously Amended) A method for modifying the glycosylation profile of a polypeptide produced by a mammalian host cell, comprising introducing into said host cell an expression vector which comprises an isolated nucleic acid comprising a sequence encoding a fusion polypeptide, wherein said fusion polypeptide has $\beta(1,4)$ -N-acetylglucosaminyltransferase III activity and comprises the Golgi localization domain of a Golgi resident polypeptide other than $\beta(1,4)$ -N-acetylglucosaminyltransferase III, and wherein said modified polypeptide has increased Fc-receptor binding or effector function as a result of said modification.

32. (Original) A method according to claim 30 or 31, wherein said polypeptide is IgG or a fragment thereof.

33. (Original) A method according to claim 32, wherein said polypeptide is IgG1 or a fragment thereof.

34. (Original) A method according to claim 32, wherein said polypeptide is a fusion protein that includes a region equivalent to the Fc region of a human IgG.

35-64. (Canceled)

65. (Previously Amended) A method for producing a polypeptide in a mammalian host cell, comprising:

a. culturing a mammalian host cell engineered to express at least one nucleic acid encoding a fusion polypeptide having $\beta(1,4)$ -N-acetylglucosaminyltransferase III activity under conditions which permit the production of a polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin, wherein said fusion polypeptide is expressed in an amount sufficient to modify the oligosaccharides in the Fc region and increase the Fc-receptor binding or effector function of said polypeptide produced by said host cell and wherein said fusion polypeptide having $\beta(1,4)$ -N-acetylglucosaminyltransferase III activity comprises the Golgi localization domain of a Golgi resident polypeptide other than $\beta(1,4)$ -N-acetylglucosaminyltransferase III; and

b. isolating said polypeptide.

66. (Currently Amended) A method according to claim 65 wherein said fusion polypeptide ~~comprises~~ consists essentially of the catalytic domain of $\beta(1,4)$ -N-acetylglucosaminyltransferase III and the Golgi localization domain of a Golgi resident polypeptide other than $\beta(1,4)$ -N-acetylglucosaminyltransferase III.

67. (Cancelled)

68. (Currently Amended) A method according to claim ~~67~~65, wherein said Golgi localization domain is the localization domain of mannosidase II and wherein said produced polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin exhibits at least 15% greater antibody-dependent cellular

cytotoxicity compared to polypeptides produced in a host cell expressing wild-type $\beta(1,4)$ -N-acetylglucosaminyltransferase III.

69-73. (Canceled)

74. (Previously Amended) A method according to claim 65, wherein said increased effector function is increased Fc-mediated cellular cytotoxicity.

75-81. (Canceled)

82. (Original) A method according to claim 65, wherein said polypeptide produced by said host cell exhibits increased Fc receptor binding affinity as a result of said modification.

83. (Original) A method according to claim 82, wherein said Fc receptor is Fc activating receptor.

84. (Original) A method according to claim 82, wherein said Fc receptor is Fc γ RIIIA receptor.

85. (Original) A method according to claim 65, wherein said polypeptide produced by said host cell has an increased proportion of bisected oligosaccharides in the Fc region of said polypeptide.

86. (Original) A method according to claim 65, wherein said polypeptide produced by said host cell has an increased proportion of nonfucosylated oligosaccharides in the Fc region of said polypeptide.

87. (Original) A method according to claim 86, wherein said nonfucosylated oligosaccharides are hybrid.

88. (Original) A method according to claim 86, wherein said nonfucosylated oligosaccharides are complex.

89. (Original) A method according to claim 65, wherein said polypeptide produced by said host cell has an increased proportion of bisected, nonfucosylated oligosaccharides in the Fc region of said polypeptide.

90. (Original) A method according to claim 89, wherein said bisected, nonfucosylated oligosaccharides are hybrid.

91. (Original) A method according to claim 89, wherein said bisected, nonfucosylated oligosaccharides are complex.

92. (Original) A method according to claim 89, wherein at least 20% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

93. (Original) A method according to claim 89, wherein at least 25% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

94. (Original) A method according to claim 89, wherein at least 30% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

95. (Original) A method according to claim 89, wherein at least 35% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

96-185. (Canceled)

186. (Previously Amended) A method for producing a polypeptide in a mammalian host cell, comprising:

a. culturing a mammalian host cell engineered to express at least one nucleic acid encoding a fusion polypeptide having GnT III activity and at least one nucleic acid

encoding a polypeptide having Man II activity under conditions which permit the production of a polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin, wherein said fusion polypeptide is expressed in an amount sufficient to modify the oligosaccharides in the Fc region and increase the Fc-receptor binding or effector function of said polypeptide produced by said host cell and wherein said fusion polypeptide having GnT III activity comprises the Golgi localization domain of a Golgi resident polypeptide other than GnT III; and

b. isolating said polypeptide.

187. (Canceled)

188. (Currently Amended) A method according to claim 186 wherein said fusion polypeptide ~~comprises~~ consists essentially of the catalytic domain of GnT III and the Golgi localization domain of a Golgi resident polypeptide other than GnT III.

189. (Cancelled)

190. (Currently Amended) A method according to claim 189, wherein said Golgi localization domain is the localization domain of mannosidase II and wherein said produced polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin exhibits at least 15% greater antibody-dependent cellular cytotoxicity compared to polypeptides produced in a host cell expressing wild-type $\beta(1,4)$ -N-acetylglucosaminyltransferase III.

191-205. (Canceled)

206. (Previously Amended) A method according to claim 186, wherein said polypeptide produced by said host cell has an increased proportion of bisected, nonfucosylated oligosaccharides in the Fc region of said polypeptide.

207. (Original) A method according to claim 206, wherein said bisected, nonfucosylated oligosaccharides are hybrid.

208. (Original) A method according to claim 206, wherein said bisected, nonfucosylated oligosaccharides are complex.

209. (Original) A method according to claim 206, wherein at least 20% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

210. (Original) A method according to claim 206, wherein at least 25% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

211. (Original) A method according to claim 206, wherein at least 30% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

212. (Original) A method according to claim 206, wherein at least 35% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

213-286. (Canceled)

287. (Withdrawn) A method for modifying the glycosylation profile of a polypeptide produced by a mammalian host cell, comprising introducing into said host cell an isolated nucleic acid comprising a sequence encoding a fusion polypeptide, wherein said fusion polypeptide has $\beta(1,4)$ -galactosyltransferase activity and comprises the Golgi localization domain of a Golgi resident polypeptide selected from the group consisting of: mannosidase I, mannosidase II, $\beta(1,2)$ -N-acetylglucosaminyltransferase I, $\beta(1,2)$ -N-acetylglucosaminyltransferase II, and $\alpha 1-6$ core fucosyltransferase, and wherein said

modified polypeptide has increased Fc-receptor binding or effector function as a result of said modification.

288. (Withdrawn) A method for modifying the glycosylation profile of a polypeptide produced by a mammalian host cell, comprising introducing into said host cell an expression vector which comprises an isolated nucleic acid comprising a sequence encoding a fusion polypeptide, wherein said fusion polypeptide has $\beta(1,4)$ -galactosyltransferase activity and comprises the Golgi localization domain of a Golgi resident polypeptide selected from the group consisting of: mannosidase I, mannosidase II, $\beta(1,2)$ -N-acetylglucosaminyltransferase I, $\beta(1,2)$ -N-acetylglucosaminyltransferase II, and $\alpha 1-6$ core fucosyltransferase, and wherein said modified polypeptide has increased Fc-receptor binding or effector function as a result of said modification.

289. (Withdrawn) A method for producing a polypeptide in a mammalian host cell, comprising:

- a. culturing a mammalian host cell engineered to express at least one nucleic acid encoding a fusion polypeptide having $\beta(1,4)$ -galactosyltransferase activity under conditions which permit the production of a polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin, wherein said fusion polypeptide is expressed in an amount sufficient to modify the oligosaccharides in the Fc region and increase the Fc-receptor binding or effector function of said polypeptide produced by said host cell and wherein said fusion polypeptide having $\beta(1,4)$ -galactosyltransferase activity comprises the Golgi localization domain of a Golgi resident polypeptide selected from the group consisting of: mannosidase I, mannosidase II, $\beta(1,2)$ -N-acetylglucosaminyltransferase I, $\beta(1,2)$ -N-acetylglucosaminyltransferase II, and $\alpha 1-6$ core fucosyltransferase; and
- b. isolating said polypeptide.

290. (Withdrawn) A method according to claim 214 or 215, wherein said polypeptide is IgG or a fragment thereof.

291. (Withdrawn) A method according to claim 217, wherein said polypeptide is IgG1 or a fragment thereof.
292. (Withdrawn) A method according to claim 217, wherein said polypeptide is a fusion protein that includes a region equivalent to the Fc region of a human IgG.
293. (Withdrawn) A method according to claim 216 wherein said fusion polypeptide comprises the catalytic domain of $\beta(1,4)$ -galactosyltransferase.
294. (Withdrawn) A method according to claim 216, wherein said fusion polypeptide further comprises the Golgi localization domain of a heterologous Golgi resident polypeptide.
295. (Withdrawn) A method according to claim 221, wherein said Golgi localization domain is the localization domain of mannosidase II.
296. (Withdrawn) A method according to claim 216, wherein said increased effector function is increased Fc-mediated cellular cytotoxicity.
297. (Withdrawn) A method according to claim 216, wherein said polypeptide produced by said host cell exhibits increased Fc receptor binding affinity as a result of said modification.
298. (Withdrawn) A method according to claim 224, wherein said Fc receptor is Fc activating receptor.
299. (Withdrawn) A method according to claim 224, wherein said Fc receptor is Fc γ RIIIA receptor.

300. (Withdrawn) A method according to claim 216, wherein said polypeptide produced by said host cell has an increased proportion of bisected oligosaccharides in the Fc region of said polypeptide.

301. (Withdrawn) A method according to claim 216, wherein said polypeptide produced by said host cell has an increased proportion of bisected, nonfucosylated oligosaccharides in the Fc region of said polypeptide.

302. (Withdrawn) A method according to claim 228, wherein said bisected, nonfucosylated oligosaccharides are hybrid.

303. (Withdrawn) A method according to claim 228, wherein said bisected, nonfucosylated oligosaccharides are complex.

304. (Withdrawn) A method according to claim 228, wherein at least 20% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

305. (Withdrawn) A method according to claim 228, wherein at least 25% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

306. (Withdrawn) A method according to claim 228, wherein at least 30% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

307. (Withdrawn) A method according to claim 228, wherein at least 35% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.